PATENT COOPERATION TREATY

BG

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION TO THE DESIGNATED OFFICE OF RECEIPT OF RECORD COPY

(PCT Administrative Instructions, Section 426)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as designated Office

Date of mailing (day/month/year)	**Applicant's or agent's file reference**
19 January 2000 (19.01.00)	10248/7004WO

The designated Office is hereby notified that the International Bureau has received the record copy of the international application identified below:

Applicant(s):

International application No.	:	PCT/US99/18315
International filing date	:	13 August 1999 (13.08.99)
Priority date(s) claimed	:	21 August 1998 (21.08.98)
Date of receipt of the record copy by the International Bureau	:	17 September 1999 (17.09.99)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

G. Bähr

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

RECD 27 NOV 2000
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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
10248/7004WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/18315	13/08/1999	21/08/1998
International Patent Classification (IPC) or national classification and IPC A61K31/00		
Applicant POINT THERAPEUTICS, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28/01/2000	23.11.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Schnack, A Telephone No. +49 89 2399 8149

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/18315

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-21 as originally filed

Claims, No.:

1-21 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed.

   ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

   Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
   see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-16.

because:

☒ the said international application, or the said claims Nos. 1-16 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion

could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	none
	No:	Claims	1-21
Inventive step (IS)	Yes:	Claims	none
	No:	Claims	1-21
Industrial applicability (IA)	Yes:	Claims	17-21
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following document:

D1: WO 93 08 259
D2: WO 91 16 339
D3: WO 99 62 914
D4: WO 99 38 501
D5: WO 99 28 474
D6: WO 98 50 046
D7: WO 97 11 689
D8: WO 95 15 309
D9: WO 94 03 055
D10: WO 98 25 644

Section II
Priority

D3 relates to cyclic boroproline compounds and their use in the treatment of different diseases, e.g. viral infections and cancers, (see D3, the passages indicated in the search report).

The priority application of D3, i.e. US 60/088,540 (filed on 05.06.98) appears to originate from the same applicant as the priority document of the present application, (filed on 21.08.98). Hence, pursuant to Article 8 PCT and Article 4 Paris Convention the present priority document is not a "first application" on the invention for any subject matter already disclosed in US 60/088,540 and the present priority claim to this extent would be invalid. In other words, for all embodiments of the present case that have been made available to the public in the priority document of D3, the effective date for an assessment of novelty and inventive step (Rule 64.1 PCT) is the international filing date (13.08.99) so that D4, D5 and D6 (publ. dates 05.08.99, 10.06.99 and 12.11.98 respectively) would represent prepublished prior art. The actual wording of US 60/088,540 should therefore be checked in the national/regional phase.

Section III
Non-establishment of opinion

Claims 1-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Section V

V.1. Novelty

Objections under Article 33(2) PCT:

Present claims 17-21 relate to pharmaceutical compositions comprising the present DPP-IV inhibitors. However, such compositions do not appear to be novel, (see D1, page 3, line 1 - page 9, line 12 and page 21, lines 4-30 and D2, page 17, line 28 - page 18, line 20 and the claims). In this context it is pointed out that the intended purpose of a pharmaceutical composition is not considered to be a technical feature that would distinguish such a composition from any known pharmaceutical preparation comprising the same ingredients.

Also D7 appears to disclose the present DPP-IV inhibitors as well as compositions thereof, (see D7, page 2, line 33 - page 7, line 6). Thus, the subject matter of present claims 17-21 appears to lack novelty over D7.

Present claims 1-16 relate to a method of treating diseases, which is mediated by the alteration of substrate activity, such as the diseases mentioned in present claim 13, the methods being characterized by administering a DPP-IV inhibitor as defined in the claims. D1 and D2 teaches administering the present compounds for treating e.g. autoimmune diseases and AIDS, (see D1, page 21, lines 4-30 and D2, page 17, line 27 - page 18, line 20). Since it appears that at least some autoimmune diseases as well as AIDS are conditions, which are mediated by alteration of substrate activity, the subject matter of present claims 1-16 appears to lack novelty over D1 and D2.

D7 further discloses the use of the concerned DPP-IV inhibitors for the treatment of HIV, i.e. a viral infection. Thus, the subject matter of present claims 1-16 appears to lack novelty with respect to D7.

D8 further discloses DPP-IV inhibitors for use in the treatment of diseases, which are

DPP-IV mediated, (see D8, the passages indicated in the search report). Thus, the subject matter of present claims 1-21 appears to lack novelty over D8.

Also D9 and D10 anticipate the novelty of present claims 1-21, since these documents disclose the use of DDP-IV inhibitors for the treatment of diseases, which are DPP-IV mediated, (see D9 and D10, the passages indicated in the search report.

V.2. Inventive step

Objections under Article 33(3) PCT:

The applicant appears to claim that the invention is based on an allegedly unknown effect of DPP-IV inhibitors, the effect being an efficacy in the treatment of conditions, which are mediated by the presence and activity of the substrates of DPP-IV, (cf. present application, page 12, lines 8-10). However, it appears that all the cited references in fact disclose this effect, since inhibiting the function of the enzyme is always done in order to prevent the enzyme from functioning, and preventing the enzyme from functioning is always equivalent to hindering the enzyme from reacting with its substrate. Thus, in conclusion, it appears that administration of an enzyme inhibitor is always done in order to prevent the enzyme mediated reaction, i.e. converting the substrate to its reaction product. Thus, it cannot be considered to involve an inventive step to conclude that DPP-IV inhibitors are useful in the treatment of diseases, which are caused by or associated with a decreased DPP-IV-substrate concentration in the body. The concerned diseases appear furthermore to be known to be associated with a decreased DPP-IV substrate concentration, for which reason also not this feature could contribute to an inventive step.

V.3. Industrial applicability

Remarks under Article 33(4) PCT:

For the assessment of the present claims 1-16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for

the manufacture of a medicament for a new medical treatment.

Section VI
Certain documents

The documents D3-D6 may become relevant in the subsequent national/regional phase, (see also section II of this written opinion).

Section VIII
Objections under Article 5 and 6 PCT:

Present claim 1 is unclear in that it the expression "a medical disorder mediated by the alteration of substrate activity" is unclear. The expression does not unambiguously define the concerned disorders and it rather aims at defining the scope of the claim through a desired result to be achieved instead of defining how this result is to be achieved. In other words, the expression defines the scope of the claim through a mode of action of the DPP-IV inhibitors rather than the actual medical conditions, which are treatable with the inhibitor. Such a definition is unacceptable, because the scope of the claim is not sufficiently definite. Moreover, not any substrate, (e.g. substrates for other enzymes than DPP-IV) would be influenced by the present method.

Present claim 1 is furthermore totally unclear and indefinite, because the concerned compounds are so vaguely defined, ("a compound having the formula PR, wherein P represents...") that is would cause an undue burden for the skilled man to find out, which compounds are in fact embraced by the claim.

Present claim 2 is also considered to be unclear, because R_1-R_8 are not unambiguously defined, but are also rather defined through a desired result to be achieved instead of technical features defining the radicals.

It appears that NH_3 is included in the scope of present claim 3, (n=0). It appears however not be likely or demonstrated that NH_3 have any beneficial effect on the concerned diseases.

Present dependent claims 20 and 21 are directed to a method, whereas the claims on which they depend are directed to a composition. This inconsistency leads to unclarity with regard to the category of the claims 20-21.

PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GOSZ, William G.
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, MA 02210
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

	Date of mailing *(day/month/year)* 23.11.2000
Applicant's or agent's file reference 10248/7004WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US99/18315	13/08/1999	21/08/1998

Applicant
POINT THERAPEUTICS, INC. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hundt, D Tel.+49 89 2399-8042

INTERNATIONAL SEARCH REPORT

Intern ial Application No
PCT/US 99/18315

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/00 A61K31/69 A61K38/55 A61P37/00 A61P37/08
A61P29/00 A61P35/00 A61P1/00 A61P9/10 A61P31/00
A61P31/12 A61P43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 99 62914 A (POINT THERAPEUTICS INC) 9 December 1999 (1999-12-09) abstract page 3, line 12 -page 6, line 14 page 15, line 25 -page 17, line 4 page 20, line 7 - line 12; claims; examples ---	1-21
P,X	WO 99 38501 A (DRUCKER DANIEL J ;PLAUT ANDREW G (US); BACHOVCHIN WILLIAM W (US);) 5 August 1999 (1999-08-05) abstract page 6, line 31 -page 8, line 4 page 28, line 25 -page 35, line 5; claims; examples --- -/--	1-21

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 January 2000	03/02/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Hoff, P

3

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 99 28474 A (ORAVECZ TAMAS ;GOVERNMENT OF THE UNITED STATE (US); NORCROSS MICHA) 10 June 1999 (1999-06-10) abstract page 2, line 12 - line 21 page 4, line 12 - line 25 page 22, line 1 -page 23, line 28; claims 33,37-39 ---	1,12-16
P,X	WO 98 50046 A (TUFTS COLLEGE) 12 November 1998 (1998-11-12) the whole document ---	1-21
X	WO 95 11689 A (TUFTS COLLEGE ;BACHOVCHIN WILLIAM W (US)) 4 May 1995 (1995-05-04) cited in the application the whole document ---	1-21
X	WO 93 08259 A (NEW ENGLAND MEDICAL CENTER INC ;UNIV TUFTS (US)) 29 April 1993 (1993-04-29) the whole document, in particular page 21, lines 4-30 ---	1-21
X	WO 91 16339 A (NEW ENGLAND MEDICAL CENTER INC ;UNIV TUFTS MED (US)) 31 October 1991 (1991-10-31) the whole document, in particular page 17, line 27 to page 18, line20 ---	1-21
X	WO 95 15309 A (FERRING BV ;JENKINS PAUL D (GB); JONES D MICHAEL (GB); SZELKE MICH) 8 June 1995 (1995-06-08) abstract page 1, paragraph 3 -page 6, last paragraph; claims; examples ---	1-21
X	WO 94 03055 A (US HEALTH ;UNIV TUFTS (US)) 17 February 1994 (1994-02-17) the whole document ---	1-21
X	WO 98 25644 A (1149336 ONTARIO INC ;DRUCKER DANIEL J (CA)) 18 June 1998 (1998-06-18) abstract page 2, line 15 -page 5, line 1 page 9, line 18 - line 21 page 15, line 29 -page 16, line 19; claims 1,6,7,11-18; example 6 --- -/--	1-21

INTERNATIONAL SEARCH REPORT

Intern nal Application No
PCT/US 99/18315

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	BRISTOL L A ET AL: "Inhibition of CD26 enzyme activity with pro-boropro stimulates rat granulocyte/macrophage colony formation and thymocyte proliferation in vitro" BLOOD,US,PHILADELPHIA, PA, vol. 85, no. 12, 15 June 1995 (1995-06-15), pages 3602-3609, XP002092855 ISSN: 0006-4971 abstract page 3606, right-hand column, last paragraph -page 3607, right-hand column, last paragraph ---	1-21
A	SHIODA, TATSUO ET AL: "Anti-HIV-1 and chemotactic activities of human stromal cell-derived factor 1.alpha. (SDF-1.alpha.) and SDF-1.beta. are abolished by CD26/dipeptidyl peptidase IV-mediated cleavage" PROC. NATL. ACAD. SCI. U. S. A. (1998), 95(11), 6331-6336 , XP000867405 the whole document ---	1-21
A	ORAVECZ, TAMAS ET AL: "Regulation of the receptor specificity and function of the chemokine RANTES (regulated on activation, normal T cell expressed and secreted) by dipeptidyl peptidase IV (CD26)-mediated cleavage" J. EXP. MED. (1997), 186(11), 1865-1872 , XP000870172 the whole document -----	1-21

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/ 18315

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 1-16,20,21
is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1,12-16 relate to a compound defined by reference to a desirable characteristic or property, namely "targeting moiety that binds to DPP-IV" and "reactive group that reacts a reactive center of DPP-IV". The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by its pharmacological profile. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Furthermore, present claims 2-8,17-18 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Moreover, claims 1-12,14-21 relate to the treatment of a disease which actually is not well defined. The use of the definition "medical disorder mediated by the alteration of substrate activity" in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT. The lack of clarity is such as to render a meaningful complete search impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds structurally identified in claims 9,10,11,19-21, to the diseases mentioned in claim 13 and to the general idea underlying the present invention.

Claims searched incompletely: 1-21

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr nal Application No
PCT/US 99/18315

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9962914 A	09-12-1999	NONE	
WO 9938501 A	05-08-1999	AU 2493599 A	16-08-1999
WO 9928474 A	10-06-1999	AU 1616499 A	16-06-1999
WO 9850046 A	12-11-1998	AU 7269198 A	27-11-1998
WO 9511689 A	04-05-1995	NONE	
WO 9308259 A	29-04-1993	CA 2121369 A	29-04-1993
		EP 0610317 A	17-08-1994
		JP 7504158 T	11-05-1995
		US 5462928 A	31-10-1995
WO 9116339 A	31-10-1991	AT 148130 T	15-02-1997
		CA 2080474 A	15-10-1991
		DE 69124371 D	06-03-1997
		DE 69124371 T	12-06-1997
		DK 528858 T	28-07-1997
		EP 0528858 A	03-03-1993
		ES 2099158 T	16-05-1997
		GR 3023233 T	30-07-1997
		US 5462928 A	31-10-1995
WO 9515309 A	08-06-1995	AU 1113395 A	19-06-1995
		AU 8421998 A	12-11-1998
		CA 2178066 A	08-06-1995
		CN 1141033 A	22-01-1997
		CZ 9601595 A	15-01-1997
		EP 0731789 A	18-09-1996
		FI 962315 A	05-08-1996
		HU 76274 A	28-07-1997
		JP 9509921 T	07-10-1997
		NO 962269 A	30-07-1996
		PL 314838 A	30-09-1996
		US 5939560 A	17-08-1999
		ZA 9409525 A	02-08-1995
WO 9403055 A	17-02-1994	AU 4794393 A	03-03-1994
WO 9825644 A	18-06-1998	US 5952301 A	14-09-1999
		AU 5220098 A	03-07-1998
		EP 0944396 A	29-09-1999

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		